

Linking Disease to Protein Structure Using NCBI Resources

1. From the NCBI home page (<http://www.ncbi.nih.gov>) click on OMIM.
2. Enter the disease of interest and click Go.
3. Select a record from the list.
4. Click the link on the left named “Allelic Variants.”
5. Choose a variant, and note the mutation in the protein. These will have a format such as [ALA240VAL], meaning that at residue 240 in the protein sequence an alanine (wild-type or normal protein) is changed to a valine (mutant or disease-causing protein).
6. Click on the word “LocusLink” on the left sidebar, and then click on the LocusID number (in purple).
7. Scroll down to the Reference Sequence section and find the protein record (try to find one that begins with NP_), and click on the “BL” link (stands for BLAST link).
8. From the Blink report, click the “3D Structures” button to get a list of protein records with structures.
9. Click the little blue dot next to the structure you want to view. This launches Cn3D with an alignment of your query sequence against the sequence represented by the structure.
10. Click on the mutated residue in the top row to see its position in the structure. Use Annotate in the Style menu to show the side chain of this residue: click New, give the annotation a name, click Edit Style, check protein side chains, select ball-and-stick, and choose a color. Then click Done, OK, and Done.
11. To find atoms close to a ligand (or any other part of a structure), double click any ligand atom to highlight the ligand. Then choose Select by distance... from the Show/Hide menu, then choose Residues Only to look for amino acids only or All Molecules to include ligands and metal ions, too. Set the radius in Angstroms (3-5 is typical) and click OK.